Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

In general, fungal plant diseases can be classified into two types: those caused by soilborne fungi and those caused by airborne fungi. Soilborne fungi cause some of the most widespread and serious plant diseases, such as root and stem rot caused by *Fusarium spp.* and root rot caused by *Phytophthora spp.* For example, *Phytophthora parasitica* var. *nicotiana,* a soilborne oomycete found in many tobacco growing regions worldwide, causes black shank, a highly destructive root and stem rot disease of many varieties of cultivated tobacco.

Since airborne fungi can be spread long distances by wind, they can cause devastating losses, particularly in crops which are grown over large regions. A number of pathogens have caused widespread epidemics in a variety of crops. Important diseases caused by airborne fungi are stem rust (*Puccinia graminis*) on wheat, corn smut (*Ustilago maydis*) on corn, and late blight disease (*Phytophthora infestans*) on potato and tomato. *Plasmopera viticola* is an airborne oomycete that causes downy mildew disease on grape vines. The blue mold fungus (*Peronospora tabacina*) has caused catastrophic losses in tobacco crops, particularly in the United States and Cuba.

Most of these fungal diseases are difficult to combat, and farmers and growers must use a combination of practices, such as sanitary measures, resistant cultivars, and effective fungicide against such diseases. Hundreds of millions of dollars are spent annually for chemical control of plant-pathogenic fungi. As a result, there is today a real need for new, more effective and safe means to control plant-pathogenic fungi, particularly oomycetes which are responsible for major crop loss.

Genetic engineering promises to be an effective strategy for reducing the losses associated with diseases of field crops. Several successful approaches have been reported where the constitutive expression of antimicrobial peptides such as cecropins, lysozyme, and monoclonal antibodies effectively protected plants from parasitic organisms. However successful, these approaches have limited application to food production since many of these antimicrobial peptides and plant defense molecules are potentially toxic or allergenic to humans. Thus, alternative approaches for genetically engineering disease resistance would be more desirable.

Plants posses a highly evolved pathogen surveillance system which allows for recognition of specific pathogen derived molecules known as elicitors. Elicitor recognition

results in an incompatible plant-microbe interaction, defined as the rapid activation of plant defense genes, typically resulting in the hypersensitive response and the onset of systemic acquired resistance.

The hypersensitive response is a rapid, localized necrosis that is associated with the active defense of plants against many pathogens. The hypersensitive response elicited by bacteria is readily observed as a tissue collapse if high concentrations ($\geq 10^7$ cells/ml) of a limited host-range pathogen like *Pseudomonas syringae* or *Erwinia amylovora* are infiltrated into the leaves of nonhost plants (necrosis occurs only in isolated plant cells at lower levels of inoculum). The capacities to elicit the hypersensitive response in a nonhost and be pathogenic in a host appear linked. These pathogens also cause physiologically similar, albeit delayed, necroses in their interactions with compatible hosts. Furthermore, the ability to produce the hypersensitive response or pathogenesis is dependent on a common set of genes, denoted *hrp*. Consequently, the hypersensitive response may hold clues to both the nature of plant defense and the basis for bacterial pathogenicity.

The *hrp* genes are widespread in Gram-negative plant pathogens, where they are clustered, conserved, and in some cases interchangeable. Several *hrp* genes encode components of a protein secretion pathway similar to one used by *Yersinia, Shigella*, and *Salmonella* spp. to secrete proteins essential in animal diseases. In *E. amylovora, P. syringae*, and *P. solanacearum*, *hrp* genes have been shown to control the production and secretion of glycine-rich, protein elicitors of the hypersensitive response.

The first of these proteins was discovered in *E. amylovora* Ea321, a bacterium that causes fire blight of rosaceous plants, and was designated harpin. Mutations in the encoding *hrpN* gene revealed that harpin is required for *E. amylovora* to elicit a hypersensitive response in nonhost tobacco leaves and incite disease symptoms in highly susceptible pear fruit. The *P. solanacearum* GMI1000 *PopA*1 protein has similar physical properties and also elicits the hypersensitive response in leaves of tobacco, which is not a host of that strain. However, *P. solanacearum popA* mutants still elicit the hypersensitive response in tobacco and incite disease in tomato. Thus, the role of these glycine-rich hypersensitive response elicitors can vary widely among Gram-negative plant pathogens.

Other plant pathogenic hypersensitive response elicitors have been isolated, cloned, and sequenced. These include: *Erwinia chrysanthemi, Erwinia carotovora*, *Erwinia stewartii*, and *Pseudomonas syringae* pv. *syringae*.

Because the hypersensitive response results in localized necrosis of plant tissue, it is desirable to limit expression of a heterologous hypersensitive response elicitor to certain tissues in transgenic plants. This approach is discussed generally in PCT publication

WO 94/01546 to Beer et al., but no specific transgenic plants are identified and only two suitable fungus-responsive promoters are suggested, e.g., the phenylalanine ammonia lyase and chalcone synthase promoters. No promoters responsive specifically to infection by oomycetes are identified therein.

The present invention is directed to overcoming these and other deficiencies in the art.

With regard to the restriction requirement, applicant notes that claims 1 and 2 have now been designated as linking claims. For this reason, withdrawn claims 11-21 and 45-55 have not been canceled since these claims are subject to rejoinder upon allowance of claim 1 (with respect to the elected species).

The objection to the specification as containing an embedded hypertext link is overcome by the above amendment to the specification and should therefore be withdrawn. Applicants submit that no new matter has been added.

The objections to claims 3-4, 6, 9-10, 22-23, 30, 32-34, 43-44, and 57-58 have been overcome by the above amendments and should therefore be withdrawn.

The rejection of claims 1-10, 22-44, and 56-72 under 35 U.S.C. § 112 (first paragraph) as lacking enablement is respectfully traversed.

The U.S. Patent and Trademark Office ("PTO") has taken the position that the above-identified application fails to enable the use of: (1) nucleic acid molecules encoding a hypersensitive response elicitor protein or polypeptide other than HrpN of *Erwinia amylovora* (SEQ ID NO: 4); (2) any oomycete-inducible promoter other than *gst1* of potato; and any fragments of the *gst1* promoter of SEQ ID NO: 9. Applicants respectfully disagree.

With respect to the first issue identified above, applicants submit that due to fact that HrpN of *Erwinia amylovora* is a member of an art-recognized class of proteins that share the unique ability to cause distinct plant responses, results achieved with one member of this class would be expected by one of ordinary skill in the art to be achieved with other members of this same class. In support of applicants' position, enclosed herewith is a Declaration of Zhong-Min Wei Under 37 C.F.R. § 1.132 (with attached Exhibits 1-16) ("Wei Declaration").

In plants, the hypersensitive response phenomenon results from an *incompatible* interaction between plant pathogens and non-host plants (Wei Declaration ¶ 5). These types of interactions involve, for example, a bacterial plant pathogen attempting to infect a host plant, and the host plant preventing proliferation of the pathogen by the collapse

and death, or necrosis, of plant leaf cells at the site of infection (Id.). This is distinct from a *compatible* interaction between a bacterial plant pathogen and a host plant in which the bacteria is capable of proliferation, resulting in the spread of the pathogen throughout the plant and the manifestation of disease symptoms (Id.).

Hypersensitive response elicitors within a given genus are often homologous to elicitors from different pathogenic species and strains of the same genus (Wei Declaration ¶ 6). For example, homologs of hypersensitive response elicitors from *Erwinia amylovora* and *Pseudomonas syringae* have been identified in different bacteria species and strains from the genera *Erwinia* and *Pseudomonas*, respectively (Id.). In addition, numerous reported studies confirm that a gene encoding a hypersensitive response elicitor from a particular source genus can be used to isolate a corresponding hypersensitive response elicitor gene from different species and strains of that same genus (Wei Declaration ¶ 7). For example, the *Erwinia amylovora* hypersensitive response elicitor encoding gene was used as a probe to isolate, clone, and sequence the gene encoding the *Erwinia chrysanthemi* hypersensitive response elicitor (Id.). In the same manner, the gene encoding the *Erwinia carotovora* hypersensitive response elicitor was isolated, sequenced, and cloned by using the *Erwinia chrysanthemi* hypersensitive response elicitor encoding gene to probe the genomic library of *Erwinia carotovora* (Wei Declaration ¶ 8). The gene encoding the hypersensitive response elicitor of *Erwinia amylovora* has also been used as a probe to isolate and clone the gene encoding the hypersensitive response elicitor of *Erwinia stewartii* (Wei Declaration ¶ 9). It was found that antibodies raised against the hypersensitive response elicitor of *Erwinia stewartii* cross-reacted with the hypersensitive response elicitor of *Erwinia amylovora* (Id.). Similar findings were reported for hypersensitive response elicitors from the genus *Pseudomonas* (Wei Declaration ¶ 10). An internal fragment of the hypersensitive response elicitor from *Pseudomonas syringae* pv. *syringae* (i.e., *hrpZ*) was used to identify and isolate the hypersensitive response elicitors from *P. syringae* pv. *glycinea* and *P. syringae* pv. *tomato* (Id.). Significant amino acid sequence similarities were identified between the various *Pseudomonas syringae* elicitors (Id.).

The genes encoding hypersensitive response elicitors are positioned within the *hrp* gene cluster or proximate to the *hrp* gene cluster in *hrp* regulons (Wei Declaration ¶ 11). For example, *hrpN* from *Erwinia amylovora* was located within the *hrp* gene cluster, as was *hrpZ* from *Pseudomonas syringae* (Id.). The *popA* gene, encoding a hypersensitive response elicitor from *Pseudomonas* (now Ralstonia) *solanacearum*, was located on the left flank of the *hrp* gene cluster within a *hrp* regulon (Id.). Similar to the *popA* gene, *hreX*, the gene

encoding a hypersensitive response elicitor from *Xanthomonas campestris*, was located on the left flank of the *hrp* gene cluster (Id.).

The characteristics that distinguish hypersensitive response elicitors as a distinct class of molecules are clearly apparent when considering the different elicitors' secretion mechanisms, regulation, biochemical characteristics, and biological activities (Wei Declaration ¶ 12). Substantially all hypersensitive response elicitors identified have been shown to be secreted through the type III, *hrp* dependent secretion pathway (Wei Declaration ¶ 13). The type III secretion pathway is a highly conserved and unique mechanism for the delivery of pathogenicity related molecules in gram-negative bacteria (Id.). The *hrp* gene cluster is largely composed of components of the type III secretion system (Id.). Regulation of the genes encoding the *hrp* gene cluster, and subsequently the genes encoding the components of the type III secretion system and hypersensitive response elicitors, is controlled by environmental factors (Wei Declaration ¶ 14). Specifically, transcriptional expression of these genes is induced under conditions that mimic the plant apoplast, such as low concentrations of carbon and nitrogen, low temperature, and low pH (Id.). Biochemically, hypersensitive response elicitors have a number of common characteristics (Wei Declaration ¶ 15). These include being glycine rich, heat stable, hydrophilic, lacking of an N-terminal signal sequence, and susceptible to proteolysis (Id.). These properties of the class were originally identified by He et al., "*Pseudomonas syringae* pv. *syringae* $Harpin_{PSS}$: A Protein That is Secreted via the Hrp Pathway and Elicits the Hypersensitive Response in Plants," Cell 73:1255-1266 (1993) ("He") at 1262 (copy attached hereto as Exhibit A). He is incorporated by reference in its entirety into the specification of the present application (*see* page 15, lines 20-24; page 40, lines 1-3). In addition, hypersensitive response elicitors share a unique secondary structure that has been associated with these elicitors' distinct biological activities (described below) (Wei Declaration ¶ 16). The structure has two primary components, an alpha helix unit and a relaxed acidic unit having a sheet or random turn structure (Id.). In the absence of one or both of these components, hypersensitive response elicitation does not occur (Id.).

In addition to eliciting the hypersensitive response in a broad range of plant species, hypersensitive response elicitors also share the ability to induce specific plant responses (Wei Declaration ¶ 17). The induction of plant disease resistance, plant growth enhancement, and plant stress resistance are three plant responses that result from treatment of plants or plant seeds with a hypersensitive response elicitor from a gram-negative plant pathogen (Id.).

Treatment of plants with the hypersensitive response elicitor HrpN from *Erwinia amylovora* resulted in disease resistance to a broad range of plant pathogens (Wei Declaration ¶ 18). For example, HrpN induced disease resistance to southern bacterial wilt (*Pseudomonas solanacearum*) in tomato, tobacco mosaic virus in tobacco, and bacterial leaf spot (*Gliocladium cucurbitae*) in cucumber (Id.). The hypersensitive response elicitor HrpZ from *Pseudomonas syringae* was reported to induce disease resistance in cucumber to a diverse range of pathogens, including the fungal disease *Colletotrichum lagenarium*, tobacco necrosis virus, and bacterial angular leaf spot (*Pseudomonas syringae* pv. *lachrymans*) (Wei Declaration ¶ 19).

Hypersensitive response elicitors from *Erwinia amylovora* and *Pseudomonas syringae* pv. *syringae* are also known to enhance plant growth (Wei Declaration ¶ 20). Examples 1 to 24 of U.S. Patent No. 6,277,814 to Qiu et al. showed that treatment of plants and plant seeds with HrpN from *E. amylovora* induced plant growth enhancement in species of tomato, potato, raspberry, and cucumber (Id.).

Treatment of plants with the hypersensitive response elicitor HrpN from *Erwinia amylovora* resulted in plant stress resistance (*see* Wei Declaration ¶ 27). Example 12 of U.S. Patent No. 6,277,814 to Qiu et al. and Examples 1-6 of WO 00/28055 to Wei et al. demonstrate that HrpN from *Erwinia amylovora* is capable of inducing various forms of plant stress resistance, such as chemical stress resistance, drought stress resistance, and nutritional stress resistance (Id.).

In addition to these previously reported results, experimental evidence obtained by EDEN Bioscience Corporation, as licensee of the above-identified application (*see* Wei Declaration ¶ 3), shows that other members of the art-recognized class are capable of achieving similar results. As demonstrated by the experimental evidence in paragraphs 22 and 23 of the Wei Declaration, treatment of tomato and tobacco plants with the hypersensitive response elicitor HreX from *Xanthomonas campestris* induced disease resistance in the plants against bacterial wilt and tobacco mosaic virus (Wei Declaration ¶ 21). As demonstrated by the experimental evidence in paragraphs 25 and 26 of the Wei Declaration, treatment of plants with hypersensitive response elicitors from a range of sources, such as *Pseudomonas syringae* (HrpZ) and *Xanthomonas campestris* (HreX), enhances plant growth (Wei Declaration ¶ 24). As demonstrated by the experimental evidence in paragraphs 29-33 of the Wei Declaration, treatment of plant seeds with a hypersensitive response elicitor from a diverse range of sources, such as *Erwinia amylovora* (HrpN) and *Xanthomonas campestris* (HreX), can impart salt stress resistance to plants grown from treated seeds (Wei Declaration ¶ 28).

For the foregoing reasons, one of ordinary skill in the art would expect results achieved with one hypersensitive response elicitor of the art-recognized class to be similarly achieved with all other members of the art-recognized class.

The nucleotide sequences for several hypersensitive response elicitor proteins have been previously reported in the literature (*see* Wei Declaration ¶¶ 7-11 and Exhibits thereto) and several are disclosed in the above-identified application as SEQ ID NOs: 2 (encoding $harpin_{Ech}$ or $HrpN_{Ech}$), 4 (encoding $harpin_{Ea}$ or $HrpN_{Ea}$), 6 (encoding $harpin_{Pss}$ or $HrpZ_{Pss}$), and 8 (encoding PopA1). One of ordinary skill in the art is fully able to prepare chimeric genes using these an other known members of the art-recognized class of hypersensitive response elicitors using known recombinant techniques, such as those described in the specification (paragraph bridging pages 22-23 and Example 1). As demonstrated in the above-identified application, applicants provide experimental evidence at Example 3 (pages 37-39) showing that chimeric constructs formed with an oomycete-inducible promoter and a DNA molecule encoding HrpN, a member of the art-recognized class of hypersensitive response elicitors, can impart oomycete resistance to transgenic plants that contain the chimeric gene. Because one of ordinary skill in the art can reasonably expect the results achieved using HrpN-encoding chimeric genes to be similarly achieved with chimeric genes encoding other members of the art-recognized class of hypersensitive response elicitor proteins, one of ordinary skill in the art would be fully able to prepare such chimeric genes and transgenic plants, with the plants being expected to express the chimeric gene to induce resistance to oomycetes.

The PTO cites to U.S. Patent No. 6,342,654 to Li ("Li") as evidence that a secretion signal is required for efficacy of the chimeric gene. However, Li relates to the expression of HrmA. HrmA, now known as HopPsyA, is an effector protein (*see* van Dijk et al., "The Avr (Effector) Protein HrmA (HopPsyA) and AvrPto Are Secreted in Culture from *Pseudomonas syringae* Pathovars via the Hrp (Type III) Secretion System in a Temperature- and pH-Sensitive Manner," J. Bacteriol. 181(16):4790-4797 (1999) at abstract (copy attached hereto as Exhibit B)). Avirulence and other effector proteins differ from the hypersensitive response elicitors of the art-recognized class that are useful in the present invention. Effector proteins such as HrmA (HopPsyA) function in plant cells (*see* Alfano et al., "Evidence That the *Pseudomonas syringae* pv. *syringae hrp*-Linked *hrmA* Gene Encodes an Avr-like Protein that Acts in an *hrp*-Dependent Manner Within Tobacco Cells," MPMI 10(5):580-588 (1997) at page 581, both columns (copy attached hereto as Exhibit C)) whereas the hypersensitive response elicitor proteins of the type used in the present invention function within the apoplast (Collmer et al., "Genomic Mining Type III Secretion System Effectors in

Pseudomonas syringae Yields New Picks for All TTSS Prospectors," Trends in Microbiol. 10(10):462-469 (2002) at 463, Box 1 description of "harpins" (copy attached hereto as Exhibit D)). Because HrmA, used by Li, and the art-recognized class of hypersensitive response elicitors as used in the present invention are distinct of one another, the conclusion asserted by the PTO (that a secretion signal is required for all hypersensitive response elicitors of the art-recognized class other than HrpN) is improper.

The PTO has cited no other basis for suggesting that the results demonstrated with HrpN cannot be carried out with other members of the art-recognized class of hypersensitive response elicitor proteins. Given applicants demonstration, via the Wei Declaration, that HrpN acts like other members of its art-recognized class, applicants submit that the weight of the evidence is, in fact, contrary to the PTO's assertion.

For the above reasons, the present application enables one of ordinary skill in the art to practice the claimed invention with any nucleic acid encoding a member of the art-recognized class of hypersensitive response elicitor proteins or polypeptides. Therefore, this basis of rejection is improper.

With respect to the second issue identified above, applicants submit that the recitation of the requirements of the oomycete-inducible promoter fully enables one of ordinary skill in the art to practice the present invention with *gst1* (*prp1*-1) promoter as well as any other oomycete-inducible promoters. The criteria for selecting promoters useful in accordance with the present invention is recited at page 21, lines 22-24 of the above-identified application: "The promoter of the chimeric gene should be selected on the basis of its ability to induce transcription of the first DNA molecule in response to infection of the plant by an oomycete (i.e., the oomycete activates the promoter)." Applicants submit that one of ordinary skill in the art is fully capable of identifying whether or not a given promoter is oomycete-inducible. The procedures used for determining oocymete inducibility were known in the art prior to the filing date of the present application and, therefore, need not be disclosed for purposes of enabling one of ordinary skill in the art. For example, Keller et al., "Pathogen-Induced Elicitin Production in Transgenic Tobacco Generates a Hypersensitive Response and Nonspecific Disease Resistance," Plant Cell 11:223-235 (1999) ("Keller") (already of record) reports on the use of the *hsr203J* promoter to express cryptogein in response to *Phytophthora parasitica* var. *nicotianae*. More recently, Belbahri et al., "A Local Accumulation of the *Ralstonia solanacearum* PopA Protein in Transgenic Tobacco Renders a Compatible Plant-Pathogen Interaction Incompatible," Plant J. 28(4):419-430 (2001) (copy attached hereto as Exhibit E) confirmed the breadth of the presently claimed invention by using a chimeric gene that contained the *hsr203J* promoter and a nucleic acid encoding PopA

(e.g., fragment of SEQ ID NO: 8 of the present application) to induce oomycete resistance to transgenic tobacco plants expressing the chimeric gene following oomycete infiltration. Thus, one of ordinary skill in the art can readily select previously known or hereafter developed oomycete-inducible promoters and use such promoters in accordance with the presently claimed invention. Therefore, this basis of rejection is improper.

With respect to the third issue identified above, applicants submit that the present application does, in fact, identify useful fragments of the *gst1* promoter at page 22, lines 11-17. Moreover, applicants submit that one of ordinary skill in the art can identify minimal promoter-effective regions of SEQ ID NO: 9 through no more than routine experimentation. For example, using nt 295-567 of SEQ ID NO: 9 as the starting point, one of ordinary skill in the art could readily prepare fragments thereof (i.e., nt 295-557, nt 295-547, etc. and nt 305-567, nt 315-567, etc.) and insert them into chimeric genes using known recombinant techniques, followed by transformation and screening of plants, to define the minimal promoter-effective DNA molecule that is a fragment of SEQ ID NO: 9. While numerous steps are certainly involved, this could be performed with no more than routine experimentation using known techniques and procedures. Thus, in addition to the disclosure of effective *gst1* promoter fragments defined in the present application, one of ordinary skill in the art would be fully able to identify other fragments of the *gst1* promoter. Therefore, this basis of rejection is improper.

For all of the above-noted reasons, the present application enables one or ordinary skill in the art to practice the presently claimed invention. Therefore, the rejection of claims 1-10, 22-44, and 56-72 under 35 U.S.C. § 112 (first paragraph) as lacking enablement is improper and should be withdrawn.

The rejection of claims 1-10, 22-44, and 56-72 under 35 U.S.C. § 112 (first paragraph) as lacking written descriptive support is respectfully traversed.

There appear to be two bases of rejection. First, the PTO suggests at pages 7-8 that the "...specification does not describe the sequence of any nucleic acids encoding hypersensitive response elicitor proteins from *E. amylovora* other than SEQ ID NO: 4...nor the features that distinguish *E. amylovora* hypersensitive response elicitor genes from other hypersensitive response elicitor genes." Second, the PTO suggests at page 8 that the specification does not describe effective fragments of *gst1*.

With respect to the first basis of rejection, applicants submit that the PTO must consider, for purposes of the written description requirement, all species disclosed in the present application, not just the HrpN encoding nucleic acid of *Erwinia amylovora*. As noted above, the present application identifies by sequence, four nucleic acid molecules encoding

hypersensitive response elicitor proteins derived from various bacterial plant pathogens: one encoding HrpN of *Erwinia chrysanthemi* or harpin$_{Ech}$, one encoding HrpN of *Erwinia amylovora* or harpin$_{Ea}$, one encoding HrpZ of *Pseudomonas syringae* or harpin$_{Pss}$, and one encoding PopA1 of *Pseudomonas* (now *Ralstonia*) *solanacearum*. In addition to these nucleic acid molecules, the present application identifies nucleic acid molecules from other hypersensitive response elicitor proteins derived from various bacterial plant pathogens that can be used, including the nucleic acid molecule encoding HrpN of *Erwinia carotovora* or harpin$_{Ecc}$ (page 18, lines 16-23), the nucleic acid molecule encoding HrpN of *Erwinia stewartii* or harpin$_{Est}$ (page 18, lines 23-28), and the elicitor derived from *Clavibacter michiganensis* subsp. *sepedonicus* (page 19, lines 10-13).

As demonstrated in the Wei Declaration, harpin$_{Ea}$ is a representative species of the presently recited genus and results achieved with one member of the art-recognized class have proven to be similarly achieved with other members of the art-recognized class. Thus, one of ordinary skill in the art would appreciate that the results of Example 3 in the present application, using a chimeric gene encoding harpin$_{Ea}$, fully demonstrate that applicants were in possession of the presently claimed invention using the genus of hypersensitive response elicitor proteins derived from various bacterial plant pathogens.

With respect to the second basis of rejection, applicants submit that for the same reasons noted above, the present application does demonstrate effective fragments of the *gst1* promoter as well as identifies the property that would allow one of ordinary skill in the art to select other promoters useful in accordance with the present invention. Therefore, one of ordinary skill in the art would appreciate that the results of Example 3 in the present application, using a chimeric gene formed with the *gst1* promoter, fully demonstrates that applicants were in possession of the presently claimed invention using the genus of oomycete-inducible promoters.

For all of the above-noted reasons, the present application does satisfy the written description requirement given that the application does describe a number of species that can be used in accordance with the presently claimed genus and, the results achieved using the *gst1:harpin$_{Ea}$* chimeric gene are predictive of other species within the claimed genus. The PTO has failed to provide any evidence to the contrary. Therefore, the rejection of claims 1-10, 22-44, and 56-72 under 35 U.S.C. § 112 (first paragraph) as lacking written descriptive support is improper and should be withdrawn.

The rejection of claims 6, 34, and 58-70 under 35 U.S.C. § 112 (second paragraph) for indefiniteness is respectfully traversed in view of the above amendments.

The rejection of claims 1-2, 6-7, 22-28, 30-31, 34-36, 39-41, 56-62, 64-65, 68-70, and 72 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 5,981,843 to Chappell et al. taken with the evidence of Genbank Accession U12639 is respectfully traversed.

Chappell teaches the preparation of a chimeric gene including (1) an inducible transcription regulatory sequence of the EAS4 gene (-167 to -100 nt) (col. 9, lines 36-63); (2) a promoter containing either the EAS4 promoter (col. 9, line 64 to col. 10, line 3) or a cauliflower mosaic virus 35S minimal promoter (col. 8, line 66 to col. 9, line 35); (3) a DNA molecule encoding an elicitin, a chitinase, TMV coat protein or other plant virus coat proteins, NIa virus gene, etc. (col. 10, lines 14-39 and col. 5, line 29 to col. 6, line 9); and (4) a transcription termination sequence (col. 6, lines 63-65). Chappell defines elicitins as including proteins produced by fungal plant pathogens, which proteins elicit a hypersensitive response in an infected plant (col. 5, lines 29-31) and indicates that certain bacterial proteins that also cause a hypersensitive response, such as AvrBs3 and AvrD avirulence proteins, can be considered elicitins. Chappell, notably, does not specifically recite the hypersensitive response elicitors of plant pathogenic bacteria that have been designated as "harpins" when defining other proteins that can be considered as "elicitins" for purposes of the Chappell invention. That Chappell was aware of the class of proteins designated as "harpins"—but nonetheless failed to recite them—is apparent from the recognition at col. 9, lines 54-57 that harpin proteins can serve to induce expression of the EAS4-derived inducible transcriptional regulatory sequences. Thus, Chappell's definition of elicitin does not identify the subgenus of hypersensitive response elicitors known as "harpins."

Genbank Accession U12639 is cited for disclosing that the nopaline synthase 3' regulatory sequence is present in vector pBI101.

Because Chappell fails to teach or suggest the use of harpins under control of the EAS4 promoter, Chappell cannot have anticipated the invention of claim 1. Claim 1 presently recites that the hypersensitive response elicitor protein or polypeptide is "derived from a bacterial plant pathogen" and "is characterized by being glycine rich, heat stable, hydrophilic, and capable of eliciting a hypersensitive response in plants...." As noted above, the class of art-recognized hypersensitive response elicitors from bacterial plant pathogens that have been identified in the literature as harpins are characterized by being, *inter alia*, glycine rich, heat stable, hydrophilic, and capable of eliciting a hypersensitive response in plants (He at 1262; Wei Declaration ¶ 15). Chappell fails to teach the use of such proteins. Therefore, the rejection of claims 1-2, 6-7, 22-28, 30-31, 34-36, 39-41, 56-62, 64-65, 68-70, and 72 should be withdrawn.

The rejection of claims 1-2, 6-7, 22-28, 30-31, 34-36, 39-41, 56-60, 62, 64-65, 68-70, and 72 under 35 U.S.C. § 102(a) as being anticipated by Keller is improper. As evidenced by the accompanying Declaration of Steven V. Beer Under 37 C.F.R. § 1.131 ("Beer Declaration") and Exhibit A attached thereto, the presently claimed invention was reduced to practice in the United States prior to February 1999. For this reason, Keller is not available as prior art. Therefore, the rejection is improper and should be withdrawn.

The rejection of claims 1-2, 5-10, 22-31, 34-36, 41-44, 56-60, 62-65, and 70 under 35 U.S.C. § 102(a) as being anticipated by Abdul-Kader et al., "Evaluation of the *hrpN* Gene for Increasing Resistance to Fire Blight in Transgenic Apple," Proc. of the 8th Int. Workshop on Fire Blight, Momol and Saygili, eds., Acta Horticulture 489:247-250 (1999) ("Abdul-Kader") is improper. As evidenced by the accompanying Beer Declaration and Exhibit A attached thereto, the presently claimed invention was reduced to practice in the United States prior to February 1999. For this reason, Abdul-Kader is not available as prior art. Therefore, the rejection is improper and should be withdrawn.

The rejection of claims 1-10, 22-36, 41-44, 56-65, and 70-71 under 35 U.S.C. § 103(a) for obviousness over Abdul-Kader in view of Pfitzner et al., "Isolation and Characterization of cDNA Clones Encoding Pathogenesis-related Proteins from Tobacco Mosaic Virus Infected Tobacco Plants," Nucl. Acids Res. 15:4449-4465 (1987) ("Pfitzner") is respectfully traversed. For the reasons noted above, Abdul-Kader is not available as prior art. The PTO cites to Pfitzner only for the teaching of various pathogenesis-related proteins and their secretion signals. Because Pfitzner alone fails to teach or suggest each and every limitation of the claimed invention, Pfitzner cannot have rendered obvious the invention defined by claims 1-10, 22-36, 41-44, 56-65, and 70-71. Therefore, this rejection is improper and should be withdrawn.

The rejection of claims 1-2, 5-10, 22-31, 34-38, 41-44, 56-67, and 70-71 under 35 U.S.C. § 103(a) for obviousness over Abdul-Kader in view of Scorza et al., "Producing Transgenic 'Thompson Seedless' Grape (*Vitis vinifera* L.) Plants," J. Amer. Soc. Hort. Sci. 121:616-619 (1996) ("Scorza") is respectfully traversed. For the reasons noted above, Abdul-Kader is not available as prior art. The PTO cites to Scorza only for the teaching of *Agrobacterium* and biolistic transformation of grape plant cells. Because Scorza alone fails to teach or suggest each and every limitation of the claimed invention, Scorza cannot have rendered obvious the invention defined by claims 1-2, 5-10, 22-31, 34-38, 41-44, 56-67, and 70-71. Therefore, this rejection is improper and should be withdrawn.

The rejection of claims 1-4, 6-7, 22-28, 30-33, 34-36, 39-41, 56-62, 64-65, and 68-72 under 35 U.S.C. § 103(a) for obviousness over Keller in view of Pfitzner is respectfully traversed. For the reasons noted above, Keller is not available as prior art. Because Pfitzner alone fails to teach or suggest each and every limitation of the claimed invention, Pfitzner cannot have rendered obvious the invention defined by claims 1-4, 6-7, 22-28, 30-33, 34-36, 39-41, 56-62, 64-65, and 68-72. Therefore, this rejection is improper and should be withdrawn.

The rejection of claims 1-2, 6-10, 22-28, 30-31, 34-44, 56-62, and 64-72 under 35 U.S.C. § 103(a) for obviousness over Chappell in view of Keller and further in view of U.S. Patent No. 5,977,060 to Zitter et al. ("Zitter") is respectfully traversed.

The teachings of Chappell are set forth above. For the reasons noted above, Keller is not available as prior art against the presently claimed invention. The PTO cites to Zitter only for teaching the use of *Erwinia amylovora hrpN* in transgenic plants and plant seeds, including grape plants. Because Chappell is deficient for the reasons noted above, Keller is not available as prior art, and Zitter fails to overcome the deficiencies of Chappell, the presently claimed invention cannot have been obvious over Chappell in view Zitter. Therefore, the rejection of claims 1-2, 6-10, 22-28, 30-31, 34-44, 56-62, and 64-72 should be withdrawn.

The rejection of claims 1-2, 6-10, 22-28, 30-31, 34-36, 39-44, 56-62, 64-65, 67-70, and 72 under the judicially-created doctrine of obviousness-type double patenting over Claim 16 of U.S. Patent No. 6,174,717 to Wei et al. ("Wei I") in view of U.S. Patent No. 5,776,889 to Wei et al. ("Wei II") and further in view of Chappell is respectfully traversed.

Claim 16 of Wei I recites a "transgenic plant according to claim 15, wherein the DNA molecule comprises a nucleotide sequence of SEQ ID No 4." The DNA molecule of SEQ ID NO: 4 is described by Wei I as encoding the hypersensitive response elicitor HrpN of *Erwinia amylovora*. Wei II teaches the efficacy of topically applied HrpN in controlling *Phytophthora infestans* infection of tomato seedlings. The teachings of Chappell are set forth above.

Applicants submit that the obviousness-type double patenting rejection is improper because the combination of Wei I, Wei II, and Chappell fails to suggest the use of hypersensitive response elicitors such as *Erwinia amylovora* HrpN, known as a harpin, under control of an oomycete-inducible promoter. While Chappel teaches an oomycete-inducible promoter in combination with elicitins, that may include elicitors such as Avr proteins,

Chappell fails to recognize or suggest that harpins can be used therewith. Therefore, the obviousness-type double patenting rejection is improper and should be withdrawn.

Applicants have also added new claim 73 to specify use of the *gst1* promoter. New claim 73 is similar in scope to original claim 5, which was previously indicated to be allowable over Chappell. Because claim 5 as originally filed would otherwise be allowable over the art of record, new claim 73 should be allowable.

In view of all the foregoing, it is submitted that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450, on the date below.
Date 7/30/03 Jane C. Wirszyla